

# Bilateral Deep Brain Stimulation: The Placement of the Second Electrode Is Not Necessarily Less Accurate Than That of the First One

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## Key Words

Deep brain stimulation · Electrode · Movement disorders · Parkinson's disease · Microrecording · Macrostimulation · Brain shift

## Abstract

**Background:** Deep brain stimulation (DBS) is recognized as an effective treatment for movement disorders. We recently changed our technique, limiting the number of brain penetrations to three per side. **Objectives:** The first aim was to evaluate the electrode precision on both sides of surgery since we implemented this surgical technique. The second aim was to analyse whether or not the electrode placement was improved with microrecording and macrostimulation. **Methods:** We retrospectively reviewed operation protocols and MRIs of 30 patients who underwent bilateral DBS. For microrecording and macrostimulation, we used three parallel channels of the 'Ben Gun' centred on the MRI-planned target. Pre- and post-operative MRIs were merged. The distance between the planned target and the centre of the implanted electrode artefact was measured. **Results:** There was no significant difference in targeting precision on both sides of surgery. There was more intra-operative adjustment of the second electrode positioning based on microrecording and macrostimulation, which allowed to significantly

approach the MRI-planned target on the medial-lateral axis. **Conclusion:** There was more electrode adjustment needed on the second side, possibly in relation with brain shift. We thus suggest performing a single central track with electrophysiological and clinical assessment, with multidirectional exploration on demand for suboptimal clinical responses.

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## Introduction

Deep brain stimulation (DBS) through stereotactically implanted electrodes is a well-established procedure for treatment of Parkinson's disease and other movement and psychiatric disorders involving a dysfunction of the basal ganglia. Accuracy in defining the target and the positioning of the electrodes in the deep brain structures, such as the subthalamic nucleus (STN), ventro-intermediate nucleus of the thalamus (Vim) or globus pallidus internus is crucial for the efficacy of this procedure. The precision of the targeting relies on pre-operative planning using stereotactic images and atlases, intra-operative electrophysiological microrecording and clinical testing during macrostimulation. Brain shift may occur during DBS surgery, which can compromise the final position of the implanted electrodes. The following factors have so

far been incriminated: subdural air invasion, cerebrospinal fluid loss, and gravitational force [1, 2]. A shift of a few millimetres is enough to displace the electrodes out of their target, as the STN, for example, measures 4 × 6 mm in the axial plane [3]. Also, due to the somatotopic organization and the functional segregation of these nuclei, a small electrode displacement can alter the expected clinical effect and induce adverse reactions.

Several strategies have been studied in order to decrease brain shift. Some authors discuss the possibility of using intra-operative imaging such as X-ray or MRI in order to detect brain shift [4, 5]. Others use microelectrode recording before implantation of the final electrode during DBS, in order to adjust for targeting errors and brain shift [1, 6, 7]. Petersen et al. [8] suggested sealing the dural defect as soon as possible during DBS implantation in order to limit cerebrospinal fluid outflow, while Coenen et al. [9] developed a burr hole technique which decreases cerebrospinal fluid loss and intracranial air invasion.

Surgical protocols vary highly across centres and at different steps of DBS, as described by Abosch et al. [10]. A few years ago, when we introduced the 'Ben Gun' device in our surgical technique, we decided to restrict, whenever possible, the number of brain penetrations to three per side instead of five, using a standardized method with three electrodes placed on the medial-lateral axis, in order to limit brain damage secondary to the passage of the tracks.

The first objective of this study was to evaluate the final electrode position on the first versus the second side of surgery, as well as the global electrode precision obtained in our series since we introduced this original standardized three-track procedure. The second objective was to analyse whether or not the accuracy of the electrode placement was improved by using microrecording and macrostimulation.

## Material and Methods

### Patient Demographics

We retrospectively analysed 47 consecutive patients who underwent bilateral DBS surgery for treatment of movement disorders in our institution since the introduction of our standardized technique using three electrodes placed on the medial-lateral axis for microrecording. We excluded 15 patients for whom all MRI images of both pre- and post-stereotactic implantation were not available in our database and 2 patients for whom the planned target was modified intra-operatively on the second side. The targets were the STN for the 28 patients with Parkinson's disease and the Vim for the 2 patients with essential tremor. The mean age at sur-

**Table 1.** Patient demographics

Patients (n = 30)	
Mean age, years	64.1
Gender, M/F	12/18
Movement disorders	
Parkinson's disease, n	28
Essential tremor, n	2
Bilateral procedure, n	30
DBS targets	
STN, n	28
Vim, n	2

**Table 2.** Duration of surgery (in hours)

Patients (n = 28)	
Minimum	1.27
25% percentile	3.33
Median	3.79
75% percentile	4.00
Maximum	9.45

gery was 64.1 years (table 1). The median duration of surgery was 3.79 h with an interquartile range of 3.33–4.00 (table 2). The data for 2 patients were not available.

### Surgical Procedure and Image Analysis

The patients underwent an initial pre-operative brain T2-weighted MRI on a 3-tesla magnet (Trio, Skyra and Verio 3 Tesla MRI, Siemens, Erlangen, Germany). Under local anaesthesia, a stereotactic CRW head frame (Integra Radionics, Burlington, Mass., USA) was fixed in bifrontal and biparietal positions to the patient's head. The patients underwent pre-operative MRI on a 1.5-tesla magnet (Aera 1.5 Tesla MRI, Siemens) with the secured frame on, in order to obtain an MPRAGE sequence. A neuronavigation software (FrameLink; Medtronic, Minneapolis, Minn., USA) was used to merge the MPRAGE images with the T2 3-tesla MRI images. Based on these two MRIs and the merged images, the stereotactic coordinates of the bilateral targets, which were chosen at the centre of the motor part of the subthalamus nuclei, and the trajectories of the electrodes were determined [11]. At the time of surgery, patients were placed supine in a semi-sitting position with the head and frame fixed to the operating table. Under local anaesthesia, an 8-mm burr hole was drilled on the first side of surgery at a point determined by the pre-operative planning. The dura was coagulated and opened. The three medial-lateral parallel channels of the 'Ben Gun' device (Integrated Surgical Systems, Lyon, France), 2 mm apart, were centred on the planned MRI target, and the three microelectrodes (Inomed, Emmendingen, Germany) were inserted. The three electrodes were lowered to the target area and microrecording of the three horizontal electrodes was analysed in order to determine STN localization and

borders. For Vim, microrecording detected tremor cells but did not help in delimitating the borders of the nucleus. Then, macrostimulations were performed to evaluate clinical response and side effects. For the first clinical testing, we systematically chose the electrode with the best trajectory, meaning the one with the best electrophysiological pattern as well as the longest path within the nucleus. However, if the electrophysiological and clinical results were not optimal, we explored the remaining channels on the anterior-posterior axis or even, for a few patients, the oblique areas (anterior-lateral, anterior-medial, posterior-lateral and posterior-medial) after having performed a 45° rotation of the 'Ben Gun' device. The electrode trajectory with the best ratio between electrophysiological data, clinical response at the lowest level of stimulation and least side effects has been chosen to insert the definitive Medtronic 3389 electrode for STN, and 3387 for Vim, respectively. The electrode was then fixed to the skull with cement. The same procedure was performed on the second side. Immediately after the procedure, patients underwent a control MRI with the frame on.

For each patient, pre-operative MRI with the head frame on was merged with post-operative MRI, using the FrameLink software. For each patient and in both hemispheres, it was first noted whether the electrode was in the pre-planned anatomical target or not. If not, the distance in millimetres between the pre-planned target and the centre of the implanted electrode artefact was measured in an axial plane on the medial-lateral (x) and on the anterior-posterior (y) axes. As all of the electrodes were implanted on purpose deeper than the target point (in order to 'cover' the target area) and that consequently there was always a plot at the level of the target, we did not consider the z-axis in our analysis.

For the subgroup of patients for whom there was an electrode displacement intra-operatively (another channel than the central one was chosen), we performed two analyses. First, we measured the distance between the implanted electrode and the MRI-planned target. Then, we considered the hypothetical case if the central channel had been chosen and we measured the distance between this channel and the MRI-planned target. This double analysis was performed in order to evaluate whether an intra-operative electrode displacement helped to approach the pre-planned target or not.

#### Statistical Analysis

A paired t test was used to detect significant differences between the localization of the implanted electrode compared to the MRI-planned target on both sides of the brain, considering the medial-lateral and anterior-posterior axes. The level of significance for all analyses was chosen at  $p < 0.05$ . All values were expressed as the mean  $\pm$  standard error (SE).

## Results

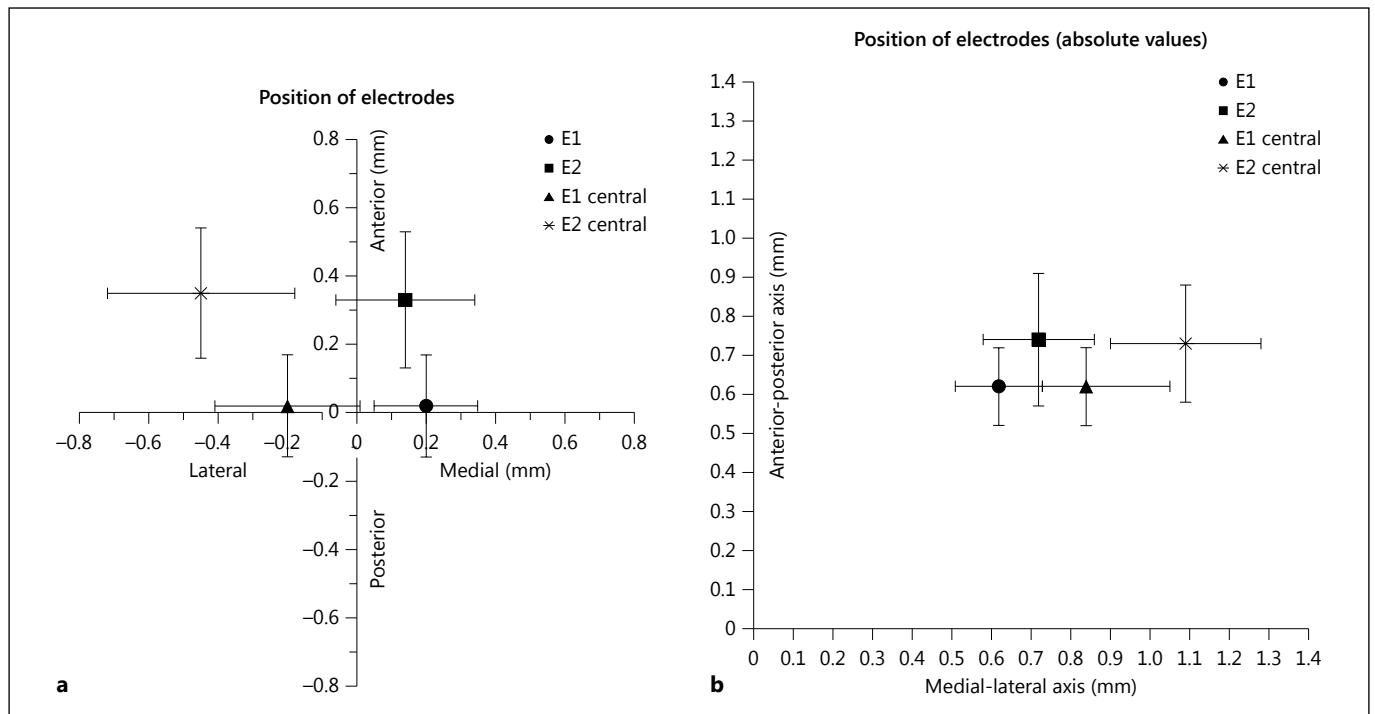
### *Where Were the Electrodes Implanted?*

Considering the localization of the implanted electrode artefact on the MRI compared to the MRI-planned target, on average, the implanted electrode on the first side was placed  $0.22 \pm 0.15$  mm medially and  $0.02 \pm$

$0.15$  mm anteriorly to the MRI-planned target, while the implanted electrode on the second side was placed  $0.14 \pm 0.19$  mm medially and  $0.33 \pm 0.20$  mm anteriorly (fig. 1a). Altogether, there was no statistically significant difference in the accuracy of the localization of the first versus the second electrode. However, there was a tendency for the second electrode to be more anterior than the target [ $t(29) = 1.67$ ;  $p = 0.11$ ] compared to the first electrode. The mean distance in absolute value for the first electrode was  $0.62 \pm 0.11$  mm on the medial-lateral axis and  $0.62 \pm 0.10$  mm on the anterior-posterior axis. The mean error of targeting on the first side was  $1.06 \pm 0.10$  mm. The mean distance in absolute value for the second electrode was  $0.72 \pm 0.14$  mm on the medial-lateral axis and  $0.74 \pm 0.17$  mm on the anterior-posterior axis. The mean error of targeting on the second electrode was  $1.30 \pm 0.17$  mm (fig. 1b). Altogether, there was no statistically significant difference in the mean distance between the MRI-planned target and the implanted electrode for the first versus the second electrode, considering the absolute values.

### *Where Would the Electrodes Have Been Located If the Central Track Had Always Been Chosen?*

Based on pre-planning MRIs, the coordinates of the bilateral targets and the trajectories of the electrodes were determined. Figure 1a shows the position of the central electrodes compared to the target on both sides. On the first side, the central electrode was localized  $0.20 \pm 0.20$  mm laterally and  $0.02 \pm 0.15$  mm anteriorly to the MRI-planned target, while the central electrode on the second side was localized  $0.45 \pm 0.26$  mm laterally and  $0.35 \pm 0.19$  mm anteriorly. On average, there was no statistically significant difference between the positions of central electrodes within the first versus second side of surgery. However, there was a tendency for the second electrode to be more anterior and lateral than the target compared to the first electrode [ $t(29) = 0.7$ ;  $p = 0.49$  on the medial-lateral axis and  $t(29) = 1.84$ ;  $p = 0.08$  on the anterior-posterior axis]. The mean distance in absolute value for the central electrode on the first side was  $0.84 \pm 0.14$  mm on the medial-lateral axis and  $0.62 \pm 0.10$  mm on the anterior-posterior axis. The mean distance in absolute value between the central electrode and the MRI-planned target (mean error of targeting) on the first side was  $1.30 \pm 0.14$  mm. The mean distance in absolute value for the central electrode on the second side was  $1.09 \pm 0.19$  mm on the medial-lateral axis and  $0.73 \pm 0.15$  mm on the anterior-posterior axis. The mean distance in ab-



**Fig. 1.** Position of implanted electrodes and central tracks. **a** Mean distances in millimetres  $\pm$  SE between the MRI-planned target and the implanted electrode on the first (E1) and the second (E2) sides of surgery, as well as between the MRI-planned target and the central electrode (E1 central for the first side and E2 central for the

second side). **b** Mean distances in millimetres (absolute value)  $\pm$  SE between the MRI-planned target and the implanted electrode on the first (E1) and the second (E2) sides of surgery, as well as between the MRI-planned target and the central electrode (E1 central for the first side and E2 central for the second side).

solite value between the central electrode and the MRI-planned target (mean error of targeting) on the second side was  $1.46 \pm 0.22$  mm (fig. 1b). Altogether, there was no statistically significant difference in the mean distance between the MRI-planned target and the central electrode for the first versus the second side of surgery, considering the absolute values.

#### *Did the Intra-Operative Electrode Position Adjustment Help in Approaching the Target?*

Figure 1a shows that, on average, if the central channel had always been chosen and no adjustment had been made during the surgery after electrophysiological and clinical testing, the central electrode would have been located significantly more laterally to the target compared to the implanted electrode [ $t(29) = 2.28$ ;  $p = 0.03$  for the first side and  $t(29) = 2.65$ ;  $p = 0.01$  for the second side]. However, there would be no difference on the anterior-posterior axis (y). Our results showed that by adjusting the position of the electrode during surgery based on

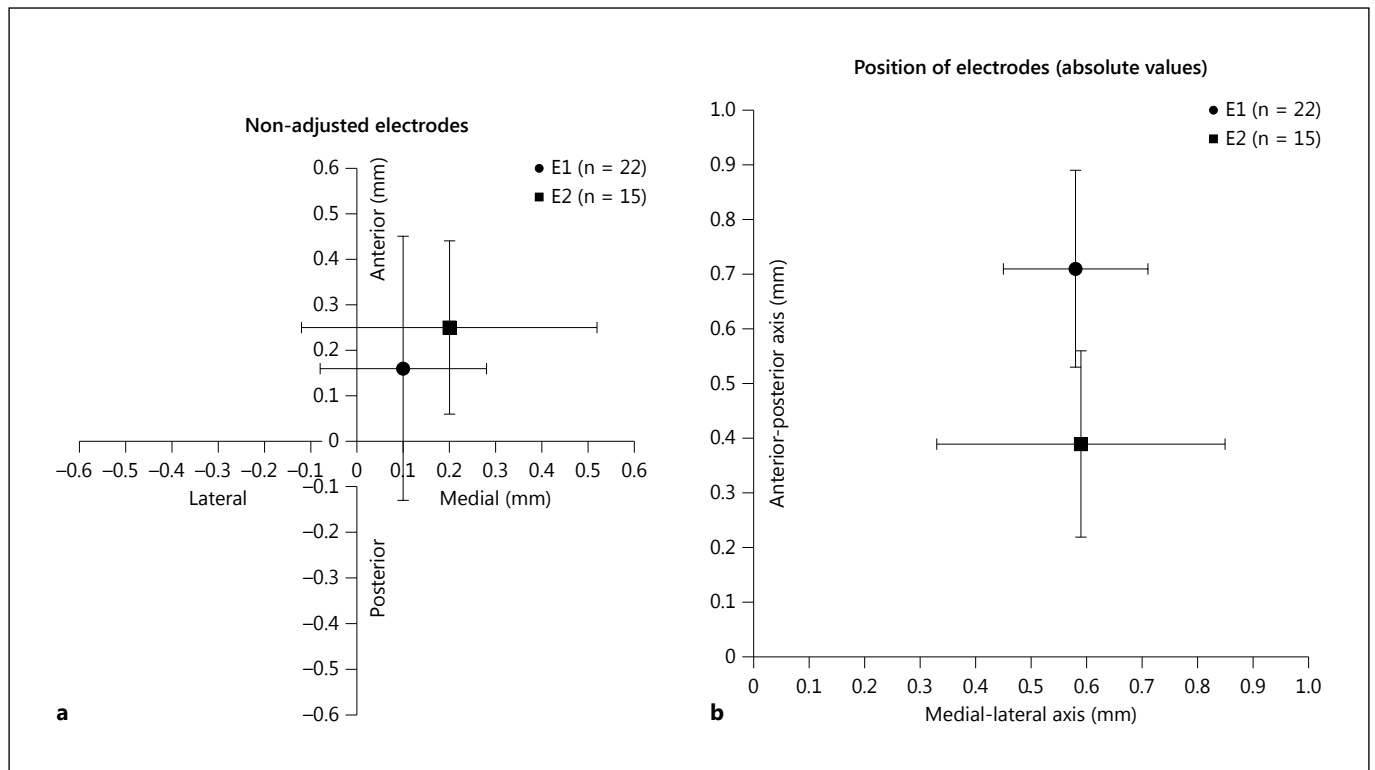
electrophysiological and clinical testing, we were able to improve the position of the implanted electrode by approaching the MRI-planned target on the second side. However, it did not make a difference on the first side.

#### *Further Subgroup Analyses*

Intra-operative microrecording and clinical testing led to electrode position adjustment in 8 patients (26.7%) on the first side and in 15 patients (50.0%) on the second side of surgery.

#### *Analysis for the Subgroup of Non-Adjusted Electrodes*

In the subgroup of electrodes whose position was not adjusted during surgery (22/30 for the first side and 15/30 for the second side), on average, the electrodes on the first side of surgery were located  $0.10 \pm 0.18$  mm medially and  $0.16 \pm 0.29$  mm anteriorly in comparison to the MRI-planned target, while the electrodes on the second side were located  $0.21 \pm 0.32$  mm medially and  $0.25 \pm 0.19$  mm anteriorly (fig. 2a). In this subgroup of electrodes whose



**Fig. 2.** Position of non-adjusted electrodes. **a** Mean distance in millimetres  $\pm$  SE between the MRI-planned target and the group of non-displaced electrodes for the first (E1) and second (E2) sides of

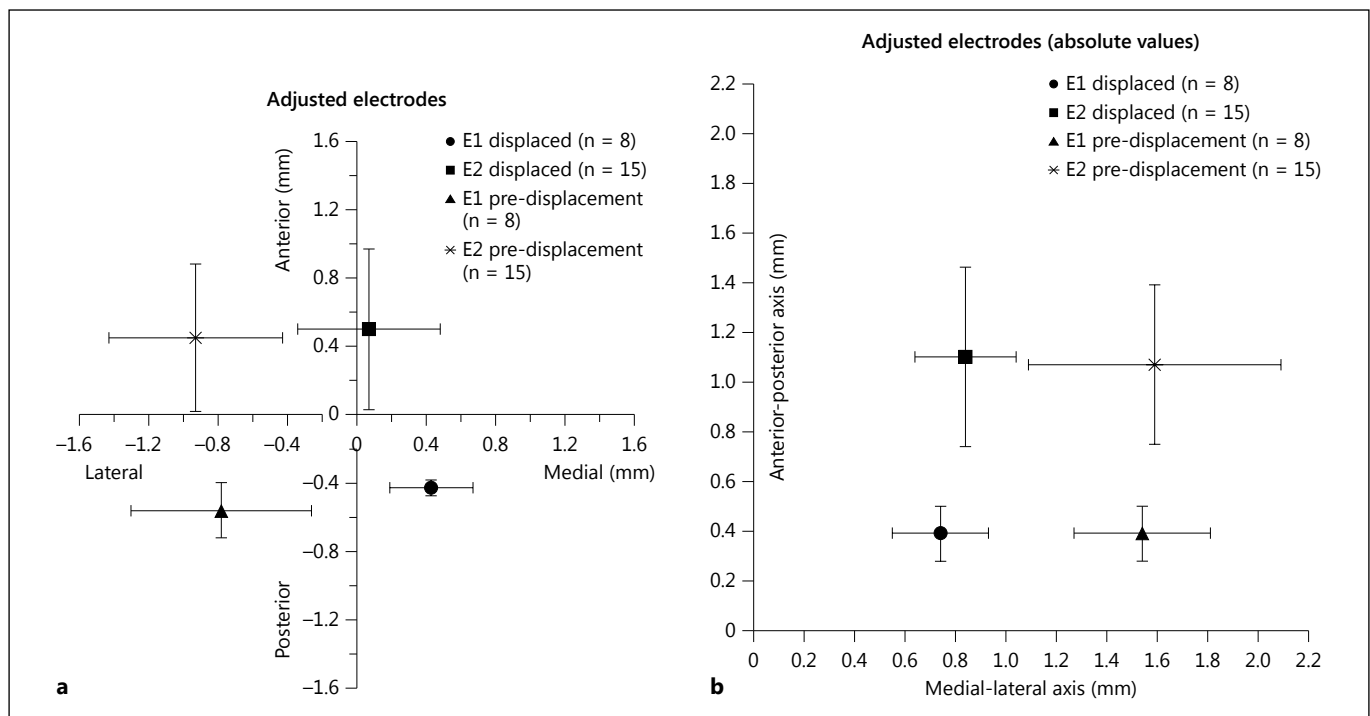
surgery. **b** Mean distance in millimetres (absolute value)  $\pm$  SE between the MRI-planned target and the group of non-displaced electrodes for the first (E1) and second (E2) sides of surgery.

position was not adjusted during surgery, there was no statistically significant difference in the position of the implanted electrodes on the first versus the second side of surgery in the medial-lateral [ $t(21) = 0.39$ ;  $p = 0.70$ ] and anterior-posterior [ $t(21) = 1.05$ ;  $p = 0.30$ ] axes.

For this subgroup, the mean distance in absolute value between the MRI-planned target and the implanted electrodes was  $0.58 \pm 0.13$  mm on the medial-lateral axis and  $0.71 \pm 0.18$  mm on the anterior-posterior axis for the first side, while it was  $0.59 \pm 0.26$  mm on the medial-lateral axis and  $0.39 \pm 0.17$  mm on the anterior-posterior axis for the second side (fig. 2b). The mean distance in absolute value between the MRI-planned target and this subgroup of electrodes whose position was not adjusted during surgery was  $1.11 \pm 0.12$  mm on the first side and  $0.85 \pm 0.27$  mm on the second side. Altogether, when considering the absolute values for this subgroup, there was no statistically significant difference in the position of the non-adjusted implanted electrodes on the first versus the second side of surgery in the medial-lateral [ $t(21) = 0.21$ ;  $p = 0.83$ ] and anterior-posterior [ $t(21) = 0.32$ ;  $p = 0.75$ ] axes.

#### *Analysis for the Subgroup of Adjusted Electrodes*

In the subgroup of electrodes whose position was adjusted intra-operatively (8/30 on the first side and 15/30 on the second side), on average, the adjusted implanted electrodes were placed  $0.54 \pm 0.26$  mm medially and  $0.39 \pm 0.11$  mm posteriorly in comparison to the MRI-planned target on the first side and  $0.07 \pm 0.38$  mm medially and  $0.41 \pm 0.49$  mm anteriorly on the second side. Moreover, in this subgroup of electrodes, if the pre-planned central channel had been chosen, these electrodes would have been placed  $1.04 \pm 0.47$  mm laterally and  $0.39 \pm 0.11$  mm posteriorly for the first side and  $1.10 \pm 0.51$  mm laterally and  $0.44 \pm 0.45$  mm anteriorly for the second side, as shown in figure 3a. Microrecording and macrostimulation helped to approach the pre-planned anatomical target in the horizontal plane, as this technique allowed to medialize the electrodes, which would have had a tendency to be placed too laterally, from 1.04 mm laterally to 0.54 mm medially on the first side and 1.10 mm laterally to 0.07 mm medially on the second side. This adjustment permitted to approach the MRI-planned target in a significant manner on both sides on



**Fig. 3.** Position of adjusted electrodes. **a** Mean distance in millimetres  $\pm$  SE between the MRI-planned target and the intra-operatively displaced implanted electrodes for the first (E1 adjusted) and second (E2 adjusted) sides of surgery. The mean distances between the MRI-planned target and the central channel, before displacement, for the first (E1 pre-adjustment) and second (E2 pre-adjustment) sides of surgery were also measured. **b** Mean distance in

millimetres (absolute values)  $\pm$  SE between the MRI-planned target and the intra-operatively displaced implanted electrodes for the first (E1 adjusted) and second (E2 adjusted) sides of surgery, as well as the mean distances in absolute value between the MRI-planned target and the central channel, before displacement, for the first (E1 pre-adjustment) and second (E2 pre-adjustment) sides of surgery.

the medial-lateral axis [ $t(7) = 3.05$ ;  $p = 0.02$  on the first side and  $t(14) = 2.94$ ;  $p = 0.01$  on the second side]. However, there was no statistically significant improvement in the position of the electrodes after adjustment on the anterior-posterior axis for the first [ $t(7) = 0$ ;  $p = 1$ ] and second sides of surgery [ $t(14) = 0.19$ ;  $p = 0.85$ ].

For this subgroup of adjusted electrodes, the mean distance in absolute value between the MRI-planned target and the implanted electrodes was  $0.74 \pm 0.19$  mm on the medial-lateral axis and  $0.39 \pm 0.11$  mm on the anterior-posterior axis for the first side of surgery, while it was  $0.84 \pm 0.26$  mm on the medial-lateral axis and  $1.1 \pm 0.36$  mm on the anterior-posterior axis for the second side (fig. 3a). The mean distance in absolute value between the MRI-planned target and this subgroup of electrodes whose position was adjusted intra-operatively (mean error of targeting) was  $0.92 \pm 0.17$  mm on the first side and  $1.75 \pm 0.27$  mm on the second side.

If the pre-planned central channel had been chosen, these electrodes would have been placed  $1.54 \pm 0.27$  mm

on the medial-lateral axis and  $0.39 \pm 0.11$  mm on the anterior-posterior axis for the first side and  $1.59 \pm 0.34$  mm on the medial-lateral axis and  $1.07 \pm 0.32$  mm on the anterior-posterior axis for the second side (fig. 3b). The mean error of targeting would have been  $1.65 \pm 0.25$  mm for the first side and  $2.06 \pm 0.40$  mm for the second side. When considering the absolute values, there was no statistically significant improvement in the position of the electrodes after adjustment on the medial-lateral axis [ $t(7) = 1.65$ ;  $p = 0.14$  for the first side and  $t(14) = 2.02$ ;  $p = 0.06$  for the second side] or the anterior-posterior axis [ $t(7) = 0$ ;  $p = 1.0$  for the first side and  $t(14) = 0.19$ ;  $p = 0.85$ ] for the second side.

## Discussion

This study showed that in our series of 30 patients operated with a standardized three-track on the medial-lateral axis technique, there was no statistically significant

difference in the position of implanted electrodes on the first versus the second side of surgery. However, adjustment rate of the second electrode position in order to approach the pre-planned target was higher.

Our results can be explained by intra-operative brain shift, already reported and described by many authors [1–3, 12–14]. Some authors have described that brain shift may be more important on the second side of surgery. Winkler et al. [14] described in a short report in 2005 the case of a 70-year-old patient who underwent bilateral STN DBS for Parkinson's disease and in whom the position of the second implanted electrode was displaced by 2 mm off the target, probably because of brain shift. The patient underwent a further operation the next day in order to replace this displaced electrode. Similarly, in 2011, a case report by Derrey et al. [15] described a patient who underwent bilateral STN DBS for Parkinson's disease and in whom there was an unsuccessful placement of the second electrode due to air invasion.

Since then, several groups have analysed and described brain shift patterns further by comparing the first and second sides of surgery, with different conclusions. On the one hand, Azmi et al. [16] described that in their series of 32 patients who underwent bilateral STN DBS, there was more deviation from the planned target, as well as more microelectrode recording tracks required for the second side of surgery.

On the other hand, Amirnovin et al. [17] described that in their series of 30 patients undergoing bilateral DBS for Parkinson's disease, the central electrode was used most often both on the first (42% of times) and the second sides of surgery (39% of times). As well, Chrastina et al. [18] described that the final electrode placement matched the anatomical trajectory in 53.4% of patients on the first side and 43.1% of patients on the second side. The difference of electrode percentages implanted did not reach a level of statistical significance. However, there was a tendency for a larger percentage of lateral electrodes on the second side.

In our study, intra-operative microrecording and macrostimulation led to electrode position adjustment in 8 patients (26.7%) on the first side and in 15 patients (50.0%) on the second side of surgery. In these patients, electrophysiology and clinical testing were successful in guiding the choice of the final electrode to approach the MRI-planned target, bilaterally, in a significant manner on the medial-lateral axis. Overall, when comparing our actual data (with electrophysiology and clinical testing, and subsequent electrode adjustment whenever needed) to the hypothetical situation in which the central channel

was always chosen (no electrophysiology or clinical testing), one can observe that there is a significant improvement in the position of the second electrode on the medial-lateral axis.

These findings are in agreement with many authors, including Priori et al. [19] and Bour et al. [20], who state that electrophysiology is an essential component in DBS for optimal targeting. Also, the correction of precision on the second side mainly affected the medial-lateral (x) axis. These results were certainly in relation with the method of microrecording and macrostimulation that we used. At the time we introduced our standardized technique using three electrodes placed on the medial-lateral axis with the 'Ben Gun' device, little was known about brain shift and more specifically the direction of it. At the time, we decided to explore the STN in its laterality. Therefore, in our study, the anterior-posterior (y) axis of the 'Ben Gun' was only rarely explored. As well, as mentioned above, we did not consider the z-axis (dorsal-ventral displacement) in our analysis. Indeed, the electrodes were implanted on purpose deeper than the target point so that there was consequently always a plot at the level of the target.

In conclusion, our study showed that microrecording and clinical testing (macrostimulation) helped to improve the position of the implanted electrodes, thus allowing us to approach the MRI-planned target. Intra-operative electrode adjustments were performed more often on the second side of surgery, thus correcting the more important deviation, secondary to brain shift. This resulted in a comparable level of accuracy in targeting on both sides of surgery.

Based on our results, we have now decided to start the surgery on the more affected hemisphere, in order to increase the chances of success on the side where the patient needs it more. Furthermore, we suggest reducing the time of surgery and as a consequence, brain shift, by performing a single central track only associated with electrophysiological and clinical assessment. With the current knowledge that we have about brain shift and more specifically its tendency to be in the posterior direction, we propose to perform multidirectional exploration in all axes (both anterior-posterior and medial-lateral) following clinical responses and side effects of stimulation, in case of suboptimal therapeutic effect.

## Disclosure Statement

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